



REVIEW ARTICLE

Tools for comprehensive evaluation of sexual function in patients with multiple sclerosis



M. Gaviria Carrillo^{a,*}, P.A. Ortiz Salas^b, K.P. Rueda Vergara^c, G.A. Cortes Bernal^c, M. Nava Mesa^d, K. Moreno Medina^e

^a Neurología, Fundación Cardio Infantil Instituto de Cardiología, Universidad del Rosario, Bogotá, Colombia

^b Neurología y Epidemiología, Fundación Cardio Infantil Instituto de Cardiología, Bogotá, Colombia

^c Neurología, Universidad del Rosario, Bogotá, Colombia

^d Grupo de investigación en Neurociencias (NEUROS), Universidad del Rosario, Bogotá, Colombia

^e Epidemiología, Fundación Cardio Infantil Instituto de Cardiología, Bogotá, Colombia

Received 4 January 2020; accepted 15 April 2020

KEYWORDS

Multiple sclerosis;
Sexual dysfunction;
Disability;
Depression;
Urodynamic function;
Quality of life

Abstract

Introduction: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system (CNS) that affects young adults, causing a variety of symptoms (motor alterations, visual alterations, loss of sphincter control, gait alterations) that impair the patient's functional status. However, other symptoms, such as sexual dysfunction, can also have an effect on quality of life.

Development: Sexual dysfunction can occur at any time during the course of the disease; its prevalence varies between 50% and 90%, and it can be secondary to demyelinating lesions in the spinal cord and/or brain or caused by symptoms that do not directly involve the nervous system (fatigue; psychological, social, and cultural factors; etc.). Although its prevalence and impact on quality of life are well known, sexual dysfunction is still frequently underestimated. Therefore, in this article we review the different scales for assessing presence or severity of sexual dysfunction, in order to offer early multidisciplinary management.

Conclusion: We evaluated 5 questionnaires that could identify the presence of sexual dysfunction in patients with MS and determine its aetiology, assisting in treatment decision making. MS must be understood as a complex disease that encompasses and compromises different aspects of patients' health, and goes beyond simply measuring disability.

© 2020 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author.

E-mail address: marigaviria8@hotmail.com (M. Gaviria Carrillo).

PALABRAS CLAVE

Esclerosis múltiple;
Disfunción sexual;
Discapacidad;
Depresión;
Función urodinámica;
Calidad de vida

Herramientas para la evaluación integral de la función sexual en pacientes con esclerosis múltiple**Resumen**

Introducción: La esclerosis múltiple (EM) es una enfermedad desmielinizante del sistema nervioso central (SNC) que afecta a adultos jóvenes, ocasionando una variedad de síntomas (motores, visuales, control de esfínteres, alteraciones de la marcha) que impactan la funcionalidad del paciente; sin embargo, otros síntomas, como la disfunción sexual (DS), también pueden tener un efecto sobre la calidad de vida.

Desarrollo: La DS puede presentarse en cualquier momento del curso de la enfermedad, su prevalencia varía entre 50 y 90%, puede ser secundaria a lesiones desmielinizantes en médula espinal y/o cerebro, ocasionada por síntomas que no incluyen directamente el sistema nervioso —fatiga, aspectos psicológicos, sociales y culturales—. Si bien se ha logrado establecer su prevalencia y su impacto sobre la calidad de vida, la DS todavía es una condición frecuentemente subestimada, razón por la cual en este artículo se revisan las diferentes escalas que ayudan a evaluar la presencia o la severidad de esta para dar un manejo multidisciplinario temprano, según corresponda.

Conclusión: Cinco cuestionarios han sido evaluados y/o diseñados para pacientes con EM, los cuales podrían identificar la presencia de DS, su etiología y, con esto, determinar posibilidades de tratamiento. La EM debe ser comprendida como una enfermedad compleja que abarca y compromete diferentes aspectos de la salud de los pacientes, y va más allá de solo medir escalas de discapacidad.

© 2020 Sociedad Española de Neurología. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system predominantly affecting adults of reproductive age (20–40 years old), mainly women. It is characterised by inflammation, demyelination, and axonal loss from early stages, which causes disability and physical and mood alterations, with a negative impact on quality of life.¹ The condition affects 2.5 million people worldwide,² with a mean prevalence of 33 cases per 100 000 people; prevalence varies from country to country, with Europe and North America presenting the highest rates.^{3,4}

Among the symptoms of MS, sexual dysfunction (SD) is a frequent concern, since sexuality has an impact on numerous aspects of daily life, including self-image, self-esteem, and interpersonal and romantic relationships. However, it has received little attention.^{2,3,5,6} SD may appear at any time over the course of MS and its prevalence ranges from 50% to 90%.² Previous studies⁴ have reported prevalence rates of 33% to 75% in women and 47% to 75% in men; however, the exact prevalence of SD is difficult to determine due to inconsistencies in its definition.^{7,8}

SD is frequently underestimated by neurologists, who tend to overlook this aspect when they evaluate patients with MS. According to a study by the Consortium of Multiple Sclerosis Centers,⁹ the most frequently evaluated symptoms (other than motor, sensory, or bowel/bladder symptoms) are depression, anxiety, sleep disorders, and pain (80%). SD is addressed with a general question in only half of cases, and physicians use a specific tool in only 4 in 24 cases, either because of time limitations or due to lack of awareness about this issue.⁹

Furthermore, few standardised and validated tools are available for the study of sexual function in MS. A systematic review by 't Hoen et al.¹⁰ identified 21 validated questionnaires for the assessment of sexual function in neurological patients, only 4 of which have been validated for use in patients with MS. However,

these tools are validated in few languages, some are only designed to assess sexual function in women, and they have not been incorporated into a comprehensive care model for patients with MS.

The purpose of this review is to describe general and specific diagnostic and follow-up tools used in studies of patients with MS and SD (scales assessing sexual function or other factors directly or indirectly affecting sexual function), with a view to proposing a more comprehensive approach to this condition, taking into account its impact on quality of life.

Sexual dysfunction

Sexual dysfunction encompasses a heterogeneous group of disorders characterised by a clinically significant alteration in a person's sexual response or capacity to experience sexual pleasure. This includes premature and delayed ejaculation, erectile dysfunction, decreased sexual desire, orgasmic dysfunction in women, genitopelvic pain, and drug-induced SD.¹¹ SD may be defined as a condition that generates anxiety and interpersonal stress for at least 6 months (except in the case of drug-induced SD).^{10,11}

The time of onset (lifelong or acquired) and form of presentation (generalised or situational) of SD must be established during assessment; these data provide diagnostic clues and may therefore have an impact on the therapeutic intervention. We should also consider other factors that may have an impact on SD, such as the partner's sexual or health problems, interpersonal problems, individual vulnerability (poor body image, history of sexual abuse), psychiatric comorbidities (depression, anxiety), stressors

(unemployment), cultural or religious factors, and medical problems. Sexual function is affected by psychological, sociocultural, and biological factors.¹¹

It has been suggested that MS may affect sexual function through various direct and indirect mechanisms; however, the exact aetiology of SD is more complex, as it involves anatomical, physiological, biological, and psychological aspects.¹¹ Foley and Iverson created a conceptual model and categorised SD in MS as primary, secondary, and tertiary dysfunction.¹²

Primary SD is caused by MS-related neurological changes that may directly affect sexual sensation and sexual response as a result of demyelinating lesions to the brain and/or spinal cord. These lesions result in loss of libido, impaired genital sensation, orgasm and arousal dysfunction, decreased vaginal lubrication, and erectile dysfunction.¹²

Secondary SD results from physical changes, rather than sequelae, that indirectly affect sexual response; it is caused by symptoms not directly involving nervous system pathways linked to the genital system. These symptoms include fatigue, weakness, spasticity, poor coordination, difficulty with mobility, bladder and bowel dysfunction, adverse drug reactions, pain, discomfort in non-genital areas, and cognitive problems.^{4,12}

Tertiary SD involves psychological, social, and cultural aspects of MS that affect sexual function; these include negative self-image, feeling less attractive, loss of confidence, fear of rejection, depression, and anger.^{12,13}

Assessment of sexual dysfunction

Patients with SD may present psychiatric comorbidities (depressive and/or anxiety disorder),¹³ urodynamic dysfunction, and poor quality of life. In the light of this, and to ensure a comprehensive evaluation of sexual function, patients should also be assessed with scales focusing on quality of life, urodynamic function, sexual satisfaction, and mood.

The evaluation of SD in patients with neurological disease should make use of validated questionnaires and tools assessing different factors with an impact on MS, either directly or indirectly: factors indirectly affecting sexual function include such physical alterations as spasticity, bladder and bowel dysfunction, adverse drug reactions, and such psychosocial problems as depression. Thorough examination contributes to a better approach to the diagnosis and treatment of SD.

Several studies have described the use of sexual function scales together with scales evaluating quality of life, urodynamic function, sexual satisfaction, and mood symptoms (Table 1).¹⁴

Scales for the assessment of sexual function in multiple sclerosis

Female Sexual Function Index

The Female Sexual Function Index (FSFI) was initially developed for non-neurological patients to evaluate specific

domains of sexual function in the preceding 4 weeks.¹⁰ It is one of the most widely used scales for the assessment of SD in women, and has even been proposed as a gold standard for the diagnosis of this condition.¹⁵

The FSFI includes 19 items, rated on a Likert-type scale from 1 to 5 according to the level of agreement.^{10,16} The domains evaluated are sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. Total score ranges from 2 to 36 points, with scores ≤ 26.55 points indicating SD.¹⁶

The scale has never been used to evaluate changes in SD after a therapeutic intervention; this is a promising field for future research. The FSFI can be used for the diagnosis and follow-up of women with MS, but is not applicable to men.

International Index of Erectile Function

The International Index of Erectile Function (IIEF) was developed and validated in 1996–1997 to evaluate the effectiveness of treatment with sildenafil in patients with SD.¹⁰

The questionnaire includes 15 questions evaluating 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Total scores range from 0 to 75 points.¹⁷

The IIEF has not yet been validated for use in neurological patients, although several studies have used it to determine the prevalence of SD in men with MS.¹⁸ It has been validated in several languages, including Spanish, and is considered the gold standard measure for efficacy assessment in clinical trials of erectile dysfunction.^{17,19}

However, it does not evaluate other domains of sexuality, such as premature ejaculation, decreased sexual desire, and relationship with the partner.^{17,18}

Sexual Dysfunction Management and Expectations Assessment in Multiple Sclerosis—Female

The Sexual Dysfunction Management and Expectations Assessment in Multiple Sclerosis—Female (SEA-MS-F) evaluates the expectations of women with MS in terms of treatment for SD. The questionnaire comprises 8 questions classified into 3 domains. The first domain addresses general expectations regarding sexuality (interest in receiving information on sexuality in MS and benefits of a treatment programme for SD); questions from the second domain enquire about specific expectations regarding SD symptoms (problems with sexual desire, excitation, pleasure, and body image); and the third domain focuses on the patient's goal in seeking treatment for SD (for their own pleasure, for their partner's pleasure, for the benefit of their relationship).²⁰ Each question is scored on a Likert-type scale, with item scores ranging from 0 to 4 and total scores ranging from 0 to 32. The questionnaire was developed and validated in a group of 40 women with MS aged older than 18 years, with Expanded Disability Status Scale (EDSS) scores < 8.5 and Mini-Mental State Examination scores > 17 , and a mean age of 48 years. It showed good psychometric properties, acceptability, and internal consistency. It was developed using the Delphi method (expert consensus).²⁰ Due to its design, the questionnaire cannot be administered to men and cannot be used to follow up patients after an intervention.

Table 1 Scales for direct assessment of sexual dysfunction and indirect assessment of other domains.

Questionnaires on SD in MS	Disability	Quality of life	Depression/ anxiety	Urodynamic function	Sexual satisfaction	Cognitive status
MSISQ-19	PDDS	MSQoL-54	BDI-II	ICIQ-FLUTS	SSS	MMSE
MSISQ-15	EDSS	SF-12	CES-D	UDI-6 short form		
SEA-MS-F	PS		HAM-A	I-QoL		
FSFI	FIM		MADRS			
	GNDS		HAM-D			
	QST					

BDI-II: Beck Depression Inventory; CES-D: Center for Epidemiological Studies-Depression; EDSS: Expanded Disability Status Scale; FIM: Functional Independence Measure; FSFI: Female Sexual Function Index; GNDS: Guy's Neurological Disability Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; ICIQ-FLUTS: International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms; I-QoL: Incontinence Quality of Life Instrument; MADRS: Montgomery Asberg Depression Rating Scale; MMSE: Mini-Mental State Examination; MS: multiple sclerosis; MSISQ-15: 15-item Multiple Sclerosis Intimacy and Sexuality Questionnaire; MSISQ-19: 19-item Multiple Sclerosis Intimacy and Sexuality Questionnaire; MSQoL-54: Multiple Sclerosis Quality of Life-54; PDDS: Patient Determined Disease Steps; PS: Performance Scales; QST: Quantitative Sensory Testing; SEA-MS-F: Sexual Dysfunction Management and Expectations Assessment in Multiple Sclerosis-Female; SD: sexual dysfunction; SF-12: 12-Item Short Form Survey; SSS: Sexual Satisfaction Survey; UDI-6 short form: Urogenital Distress Inventory, short form.

Adapted from Cordeau and Courtois.¹⁴

Szasz Sexual Functioning Scale

The Szasz Sexual Functioning Scale (SSFS) is the first questionnaire designed to evaluate sexual function and the impact of SD on the quality of life of patients with MS. It classifies patients into 5 groups according to the level of sexual activity and impact on quality of life.²¹

- Group 0: sexually active as before and/or not experiencing sexual problems (no changes in patient's usual pattern of sexual activity; for example, no changes in frequency or type of sex activities; and no changes in previous genital sensations, erections, or ejaculation in men, or vaginal lubrication and orgasm in women).
- Group 1: sexually less active than before, and/or now experiencing some sexual problems but not concerned (less frequent or less varied sexual activity; and/or some changes in previous genital sensations, erection, or ejaculation in men, or vaginal lubrication or orgasm in women, but the patient does not consider this an issue).
- Group 2: sexually less active than before and/or now experiencing some sexual problems and concerned (the patient would like to regain former sexual activity pattern and/or would like to regain previous genital sensations, erection, ejaculations, and/or orgasmic experiences).
- Group 3: sexually inactive but still concerned (sexual activity has ceased for weeks, months, or years, but the patient still wishes to regain previous pattern and functional ability).
- Group 4: sexually inactive and not concerned (given up: sexual activity has ceased for several weeks, months, or years, but the patient does not consider this an issue).

The questionnaire was validated in 1984 in a group of 73 patients, 45% of whom were less sexually active or were sexually inactive since diagnosis of MS; 27% of patients expressed concern about this situation.²¹

The SSFS does not identify the nature of the sexual problem. As a result, it cannot be used to guide treatment; it only enables clinicians to evaluate a patient's sexual func-

tion and the impact of sexual problems on their quality of life. Nonetheless, it may be used for patient follow-up with a view to determining whether SD has changed and whether some type of intervention is needed.²¹

Multiple Sclerosis Intimacy and Sexuality Questionnaire (19 items)

The 19-item Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19) evaluates the impact of MS symptoms on sexual activity, satisfaction, and overall quality of sexual relationships over the preceding 6 months. It is a self-administered questionnaire containing 19 items evaluating primary, secondary, and tertiary SD.²² It is structured as follows:

- Primary SD (5 items): less feeling or numbness in the genital area, lack of sexual interest or desire, less intense or pleasurable orgasms or climaxes, excessive time to reach orgasm or climax, and inadequate vaginal wetness or lubrication in women and difficulty getting or keeping a satisfactory erection in men.²²
- Secondary SD (9 items): muscle tightness or spasms in arms, legs, or body; bladder or urinary symptoms; bowel symptoms; feelings of dependency because of MS; tremor or shaking in hands or body; pain, burning, or discomfort; problems moving one's body as desired during sexual activity; problems with concentration, memory, or thinking; and exacerbation or significant worsening of MS.²²
- Tertiary SD (5 items): feeling that one's body is less attractive, feeling less masculine or feminine due to MS, fear of being rejected sexually because of MS, worries about sexually satisfying one's partner, and feeling less confident about one's sexuality due to MS.²²

Each item is scored from 1 to 5 (1=never, 2=rarely, 3=occasionally, 4=almost always, 5=always). Scores are proportional to the impact of SD on patients' lives; scores of 4 or 5 on an item should be analysed and discussed with

the physician. The total score is the sum of all item scores, and ranges from 19 to 95, with higher scores indicating more severe SD.^{10,22}

The questionnaire was designed by Sanders et al.²² in 2000 and was applied to 155 patients with MS in New York, 70% of whom were women, with a mean age of 45.4 years (standard deviation: 10.53). It showed good internal consistency both for total score and for domain scores; this self-administered questionnaire is therefore a valid, reliable, easy-to-administer, and practical tool for assessing the impact of MS symptoms on sexual function. However, the study presents several limitations, mainly the small size of the sample, the small percentage of men included, and the lack of cultural diversity of the sample (all participants were residents of New York). In response to the latter limitation, 2 subsequent studies have validated the questionnaire in culturally different populations.¹⁰

A study conducted in Brazil included 134 patients with MS from the Centre of Care and Treatment of Multiple Sclerosis in São Paulo, 99 of whom were women, and a group of 70 controls.²³ The researchers found that 54.3% of men and 71.1% of women with MS had some level of SD, defined as a score > 30 on the MSISQ-19 or a score of 4 or 5 on any item, and concluded that the questionnaire is a reproducible, reliable, and valid tool for assessing SD in patients with MS in the Brazilian population.²¹

A study performed in Iran, including 226 patients with MS scoring < 8 on the EDSS, with a mean age of 35.77 years (standard deviation: 8.07) and mean disease duration of 1.84 years, concluded that the MSISQ-19 is reliable and valid for the assessment of SD in Iranian women with MS. However, the questionnaire was only administered to women; further research is therefore needed to determine its usefulness in men.²⁴

The MSISQ-19 enables patients and clinicians to focus on the most severely affected sexual domain (primary, secondary, tertiary SD) in order to design a targeted intervention. For example, the cause of SD may be linked to a patient's perceived body image, and this requires a different approach from that needed for a patient whose SD is the result of MS-related spasticity.

The instrument was recently used in patients with SD and under treatment with natalizumab, showing improvements in MSISQ-19 scores 24 weeks after treatment onset; this is the only study conducted to date that evaluates the impact of disease-modifying therapy on SD.²⁵

Multiple Sclerosis Intimacy and Sexuality Questionnaire (15 items)

The 15-item Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-15) is a shorter version of the MSISQ-19; it evaluates primary, secondary, and tertiary SD with 15 questions, with the added benefit that its validation included men and women with normal sexual function.¹² The MSISQ-15 was designed in the United States in English in a study including 6299 patients with MS from the NARCOMS registry; mean age was 50 years (standard deviation: 9.63) and 75% were women. The researchers concluded that both the total scale and all subscales present good internal consistency. They also observed an association between MSISQ-15

and the 12-Item Short Form Survey, a quality of life scale; this reflects an association between psychological stress and SD, with psychological factors having the greatest impact on tertiary SD (body image issues, anxiety, etc).¹² Table 2 compares the SD assessment scales currently available.

Table 3 provides data on several recent studies applying these scales and reporting different prevalence rates.^{26–37}

Complementary scales for comprehensive evaluation of patients with sexual dysfunction

Quality of life scales

Quality of life scales are increasingly used in the assessment of disease progression and treatment, and to evaluate the care provided to patients with MS. Quality of life is frequently evaluated with self-administered questionnaires.

To understand and explore the effectiveness of any intervention in the management of MS, we need tools that are robust, valid, reliable, and universal. To date, several general tools have been used to evaluate quality of life in different populations; disease-specific instruments focus on particular problems and are more sensitive for detecting and quantifying small changes.³⁸

In clinical practice, MS-specific questionnaires are more appropriate as they are more sensitive for detecting changes in quality of life than such generic questionnaires as the 36-Item Short Form Survey. The latter provides an overview of an individual's general health status and can be applied both to patients and to the general population.

To evaluate health-related quality of life in the general population and in specific subgroups, useful approaches include comparing the burden of certain diseases, detecting health benefits caused by a wide range of treatments, and evaluating the health status of individual patients.^{39,40}

Several quality of life assessment instruments have been validated for use in patients with MS. Some of these have been used in the assessment of SD, demonstrating the negative impact of this condition on quality of life.⁴¹

Some MS-specific questionnaires are the following: Multiple Sclerosis Quality of Life-54 (MSQoL-54),⁴² Functional Assessment of Multiple Sclerosis (FAMS),⁴³ Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS),⁴⁴ Quality of Life Index-Multiple Sclerosis (QLI-MS),⁴⁵ Multiple Sclerosis Quality of Life Inventory (MSQLI),⁴⁶ Leeds Multiple Sclerosis Quality of Life (LMSQOL),⁴⁷ Multiple Sclerosis Impact Scale (MSIS-29),⁴⁸ Disability and Impact Profile (DIP),⁴⁹ Quality-adjusted Time without Symptoms and Toxicity of Treatment (Q-TWiST),⁵⁰ and Multiple Sclerosis International Quality of Life (MusiQoL).⁵¹

Disability scales

Another important aspect contributing to SD is disability, defined as motor, sensory, cognitive, walking, or sphincter-related limitations resulting from relapses or disease progression and affecting sexual function. In addition to the EDSS, the most frequently used scale for the assess-

Table 2 Summary of sexual dysfunction assessment scales validated in patients with multiple sclerosis.

Sexual dysfunction scales	FSFI	MSISQ-19	MSISQ-15	SEA-MS-F	SSFS
Sex	Women	Women/men	Women/men	Women	Women/men
Validated languages	English	Persian, Portuguese, English	English	English, French	English
Self-administered	Yes	Yes	Yes	Yes	No (administered by physician)
For post-intervention follow-up	Yes	Yes	Yes	No	Yes
For initial assessment of SD	Yes	Yes	Yes	Yes	Yes
Identifies the type of SD	Yes	Yes	Yes	No	No
Limitations	Only applicable to women	Validation in a small sample	Unable to determine whether the evaluated domains are related with MS	Not suitable for follow-up. Must be applied after EDSS and MMSE. Only applicable to women	Does not identify the affected sexual domain. Not suitable for follow-up

EDSS: Expanded Disability Status Scale; FSFI: Female Sexual Function Index; MMSE: Mini-Mental State Examination; MSISQ-15: 15-item Multiple Sclerosis Intimacy and Sexuality Questionnaire; MSISQ-19: 19-item Multiple Sclerosis Intimacy and Sexuality Questionnaire; SEA-MS-F: Sexual Dysfunction Management and Expectations Assessment in Multiple Sclerosis-Female; SD: sexual dysfunction; SSFS: Szasz Sexual Functioning Scale.

Table 3 Description of several recent studies using different scales for the assessment of sexual dysfunction.

Author	Sample (N)	Sex	Mean age in years (\pm standard deviation)	Tool used	Prevalence of SD
Balsamo et al., ²⁶ 2017	101	M: 100%	41.2 \pm 11.6	IIEF-15	74.2%
Dehghan-Nayeri et al., ²⁷ 2017	182	W: 100%	36.9 \pm 8.1	MSISQ-19	81.9%
Bartnik et al., ⁴ 2017	86	W: 100%	32.03 \pm 7.2	FSFI	27.2%
Camargo et al., ²⁸ 2018	65	W: 72% M: 28%	Median: 39 (Q ₁ -Q ₃ : 33-47)	MSISQ-19	20.0%
Masmoudi et al., ²⁹ 2018	26	W: 100%	37.73 \pm 8.16	FSFI	69.2%
Nasimbera et al., ³⁰ 2018	12	W: 66% M: 34%	53.8 \pm 11.24	FSFI IIEF-5	16.7% mild SD 16.7% severe SD
Domingo et al., ³¹ 2018	162	W: 77% M: 23%	45.6 \pm 9.5	MSISQ-19	64.2%
Hösl et al., ³² 2018	83	W: 100%	Median: 36.2 (Q ₁ -Q ₃ : 29.3-42.5)	FSFI	44.6%
Konstantinidis et al., ³³ 2019	248	W: 100%	45.8 \pm 8.4	FSFI	64.5%
Tomé et al., ³⁴ 2019	41	M: 100%	41.1 \pm 9.9	IIEF-15	74.4%
Gava et al., ³⁵ 2019	153	W: 100%	47.3 \pm 10.5	FSFI	42%
Ghasemi et al., ³⁶ 2019	260	W: 100%	37.83 \pm 7.34	MSISQ-19	76.2%
Nazari et al., ³⁷ 2020	300	W: 100%	36.35 \pm 7.33	FSFI	69.8%

FSFI: Female Sexual Function Index; IIEF-15: 15-item International Index of Erectile Function; IIEF-5: 5-item International Index of Erectile Function; M: men; MSISQ-19: 19-item Multiple Sclerosis Intimacy and Sexuality Questionnaire; SD: sexual dysfunction; W: women.

ment of disability in MS, other scales are frequently included in the evaluation of patients with MS:

- EDSS: evaluates neurological alterations in 8 functional central nervous system components: pyramidal, cerebellar, brainstem, sensory, bowel/bladder, visual, cerebral, and other.¹⁴
- Patient Determined Disease Steps (PDDS): patient-reported outcome of disability in individuals living with MS. This tool is linked to the EDSS, given that PDDS scores can be converted into EDSS scores.^{5,14,52}
- Functional Independence Measure (FIM): a measure of care burden and patient satisfaction with life. It includes an assessment of social cognition and communication.¹⁴
- Guy's Neurological Disability Scale (GNDS). It evaluates 12 domains: cognition, mood, vision, speech, swallowing, upper limb, lower limb, bladder function, bowel function, sexual function, fatigue, and other (pain, spasms, vertigo, etc).⁵³ The level of disability in each domain is established according to its severity and impact on the patient, judged according to the help required to perform these functions. The sexual function domain includes 6 yes/no questions, addressing loss of sexual desire; problems satisfying oneself/partner; sexual function alterations causing pain, spasms, or altered genital sensation; erection/ejaculation problems in men; lubrication/orgasm problems in women; and physical or sexual problems preventing sexual activity. Scoring on this domain is as follows: 0=normal sexual function or individuals who are voluntarily celibate; 1=reduced sexual interest; 2=problems satisfying oneself or sexual partner; 3=physical problems interfering with but not preventing sexual activity; 4=autonomic problems interfering with but not preventing sexual activity; 5=physical or autonomic problems totally preventing sexual activity.^{14,53}

Mood symptoms

Various studies report an association between MS and depression, as depression contributes to SD and vice versa.¹³ Depression scales used in the context of MS include the following:

- Beck Depression Inventory (BDI): a self-assessment questionnaire mainly evaluating clinical symptoms of sadness and intrusive thoughts associated with depression. This scale evaluates the highest percentage of cognitive symptoms, and does not evaluate motor or anxiety symptoms. It is frequently used to evaluate disease severity.⁵⁴
- Hamilton Depression Rating Scale (HAM-D): a scale designed to be administered by a healthcare professional, measuring the intensity or severity of depression. It is one of the most frequently used tools to monitor symptom progression in both clinical and research settings. Most items enquire about the patient's feelings at the time of assessment, except for items on sleep, which enquire about the last 2 days. The original version comprises 21 items. Shorter versions have been developed, including a 17-item version, also by Hamilton, and 24-item and 6-item versions.⁵⁴

- Montgomery Asberg Depression Rating Scale (MADRS): this scale, developed in 1979, contains 10 items that evaluate depression symptoms and their severity, based on the Comprehensive Psychopathological Rating Scale (CPRS). It is designed for administration by a healthcare professional.⁵⁴
- Center for Epidemiological Studies-Depression (CES-D): a screening tool that detects depression based on the presence of depressive symptoms over the previous week.⁵⁵

Urodynamic function

Urogenital system alterations may have a direct impact on sexual function. Some of the most frequently used scales for the detection of urodynamic dysfunction are the following:

- International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS), a self-administered questionnaire evaluating female lower urinary tract symptoms and their impact on quality of life.⁵⁶
- Urogenital Distress Inventory (UDI-6): a tool evaluating the presence, type, and severity of urinary incontinence, and the associated urogenital symptoms.⁵⁷
- Incontinence Quality of Life Instrument (I-QoL). This tool comprises 3 subscales: avoidance and limiting behaviours, psychosocial impact, and social embarrassment.⁵⁸

Conclusion

Although many scales have been developed to evaluate SD, only 5 have been validated in and/or designed specifically for patients with MS. These instruments may help us to detect SD, establish its aetiology, and identify possible treatments. In view of the high prevalence of SD in patients with MS and its considerable impact on quality of life, all patients should undergo a thorough examination of sexual function, evaluating such domains as mood, disability, and urodynamic function.^{10,14,59}

This review not only provides information on the scales available to date, but also gives a general overview of the factors contributing to SD, which are complex and difficult to manage. These scales provide valuable information for therapeutic decision-making.

Future studies should use these questionnaires to evaluate patient response to treatment for SD and aim to determine whether disease-modifying treatments for MS have an impact on SD.

MS must be recognised as a complex entity involving numerous health domains, in addition to the associated disability.

References

1. Vidal-Jordana A, Montalban X. Multiple Sclerosis: epidemiologic, clinical, and therapeutic aspects. *Neuroimaging Clin N Am*. 2017;27:195–204. <http://dx.doi.org/10.1016/j.nic.2016.12.001>.
2. Karamyan A, Sellner J. Journal Club: effect of comorbidity on mortality in multiple sclerosis. *Neurology*. 2016;86:e228–30. <http://dx.doi.org/10.1212/WNL.0000000000002718>.
3. Thompson AJ, Baranzini SE, Geurts J, Hemmer B, Ciccarelli O. Multiple sclerosis. *Lancet*. 2019;391:1622–36. [http://dx.doi.org/10.1016/S0140-6736\(18\)30481-1](http://dx.doi.org/10.1016/S0140-6736(18)30481-1).
4. Bartnik P, Wielgoś A, Kacperczyk J, Piszczak K, Szymusik I, Podlecka Pietowska A, et al. Sexual dysfunction in female

- patients with relapsing-remitting multiple sclerosis. *Brain Behav.* 2017;7:e00699, <http://dx.doi.org/10.1002/brb3.699>.
5. Marck CH, Jelinek PL, Weiland TJ, Hocking JS, De Livera AM, Taylor KL, et al. Sexual function in multiple sclerosis and associations with demographic, disease and lifestyle characteristics: an international cross-sectional study. *BMC Neurol.* 2016;16:210, <http://dx.doi.org/10.1186/s12883-016-0735-8>.
 6. Schairer LC, Foley FW, Zemon V, Tyry T, Campagnolo D, Marrie RA, et al. The impact of sexual dysfunction on health-related quality of life in people with multiple sclerosis. *Mult Scler.* 2014;20:610–6, <http://dx.doi.org/10.1177/1352458513503598>.
 7. Dupont S. Multiple sclerosis and sexual functioning — a review. *Clin Rehabil.* 1995;9:135–41, <http://dx.doi.org/10.1177/026921559500900208>.
 8. Celik DB, Poyraz EÇ, Bingöl A, Idiman E, Ozakbaş S, Kaya D, et al. Sexual dysfunction in multiple sclerosis: gender differences. *J Neurol Sci.* 2013;324:17–20, <http://dx.doi.org/10.1016/j.jns.2012.08.019>.
 9. Griswold GA, Foley FW, Halper J, LaRocca NG, Zemon V. Multiple sclerosis and sexuality: a survey of MS Health professionals' comfort, training, and inquiry about sexual dysfunction. *Int J MS Care.* 2003;5:37–51.
 10. 't Hoen LA, Groen J, Scheepe JR, Reuvers S, Diaz DC, Padilla Fernández B, et al. A quality assessment of patient-reported outcome measures for sexual function in neurologic patients using the consensus-based standards for the selection of health measurement instruments checklist: a systematic review. *Eur Urol Focus.* 2016;3:444–56, <http://dx.doi.org/10.1016/j.euf.2016.06.009>.
 11. McCabe MP, Sharlip ID, Atalla E, Balon R, Fisher ADLE, Laumann E, et al. Definitions of sexual dysfunctions in women and men: a consensus statement from the fourth international consultation on sexual medicine 2015. *J Sex Med.* 2016;13:135–43.
 12. Foley FW, Zemon V, Campagnolo D, Marrie RA, Cutter G, Tyry T, et al. The Multiple Sclerosis Intimacy and Sexuality Questionnaire — re-validation and development of a 15-item version with a large US sample. *Mult Scler J.* 2013;19:1197–203, <http://dx.doi.org/10.1177/1352458512471876>.
 13. Pöttgen J, Rose A, van de Vis W, Engelbrecht J, Pirard M, Lau S, et al. Sexual dysfunctions in MS in relation to neuropsychiatric aspects and its psychological treatment: a scoping review. *PLoS One.* 2018;13:e0193381.
 14. Cordeau D, Courtois F. Sexual disorders in women with MS: assessment and management. *Ann Phys Rehabil Med.* 2014;57:337–47, <http://dx.doi.org/10.1016/j.rehab.2014.05.008>.
 15. Borello-france D, Leary MO, Okonski J, Cannon-smith T. Test-retest reliability of the Urge-Urinary Distress Inventory and Female Sexual Function Index in women with multiple sclerosis. *Urol Nurs.* 2008;28:30–5.
 16. Hatzichristou D, Kirana PS, Banner L, Althof SE, Lonnee-Hoffmann R, Dennerstein L, et al. Diagnosing sexual dysfunction in men and women: sexual history taking and the role of symptom scales and questionnaires. *J Sex Med.* 2016;13:1166–82, <http://dx.doi.org/10.1016/j.jsxm.2016.05.017>.
 17. Rosen RC, Cappelleri JCGN. The International Index of Erectile Function (IIEF): a state-of-the-science review. *Int J Impot Res.* 2002;14:226–44.
 18. García L, Velazquez A, Bellosta E, Santos S, Iniguez C. Sexual dysfunction in male patients with Multiple Sclerosis (P2.183). *Neurology.* 2016;86 16 Suppl. P2.183.
 19. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology.* 1997;49:822–30.
 20. Bisseriex H, Guinet-Lacoste A, Chevret-Méasson M, Costa PSIS. Sexual Dysfunction Management and Expectations Assessment in Multiple Sclerosis-Female (SEA-MS-F): creation and validation of a specific questionnaire. *J Sex Med.* 2014;11:2955–65, <http://dx.doi.org/10.1111/jsm.12706>.
 21. Szasz G, Paty D, Lawton-Speert SEK. A Sexual Functioning Scale in multiple sclerosis. *Acta Neurol Scand Suppl.* 1984:37–43.
 22. Sanders AS, Foley FW, Larocca NG, Zemon V. The multiple sclerosis intimacy and sexuality questionnaire-19 (MSISQ-19). *Mult Scler.* 2000;18:3–27.
 23. da Silva RAP, do Olival GS, Stievano LP, Toller VB, Jordy SS, Eloi M, et al. Validação e adaptação transcultural da escala modificada de disfunção sexual em esclerose múltipla na população Brasileira. *Arq Neuropsiquiatr.* 2015;73:681–7, <http://dx.doi.org/10.1590/0004-282X20150078>.
 24. Mohammadi K, Rahnema P, Montazeri A, Foley FW. The multiple sclerosis intimacy and sexuality questionnaire-19: reliability, validity, and factor structure of the persian version. *J Sex Med.* 2014;11:2225–31, <http://dx.doi.org/10.1111/jsm.12531>.
 25. Robertson D, Aungst A, Collier R, Vivar J, Moreo N, Casady L, et al. Patient perceived changes in sexual dysfunction after initiation of natalizumab for multiple sclerosis. *Mult Scler J Exp Transl Clin.* 2018;4:055217318781989.
 26. Balsamo R, Arcaniolo D, Stizzo M, Illiano E, Autorino R, Natale F, et al. Increased risk of erectile dysfunction in men with multiple sclerosis: an Italian cross-sectional study. *Cent Eur J Urol.* 2017;70:289–95, <http://dx.doi.org/10.5173/cej.2017.1380>.
 27. Dehghan-Nayeri N, Khakbazan Z, Ghafoori FNS. Sexual dysfunction levels in Iranian women suffering from multiple sclerosis. *Mult Scler Relat Disord.* 2017;49–53, <http://dx.doi.org/10.1016/j.msard.2017.01.005>.
 28. Camargo A, Lopez A, Hernandez LPL. Symptoms present in multiple sclerosis: case series. *Acata Neurol Colomb.* 2018:108–14, <http://dx.doi.org/10.22379/24224022198>.
 29. Masmoudi R, Aissi M, Halouani N, Fathallah S, Louribi I, Aloulou J, et al. Female sexual dysfunction and multiple sclerosis: a case-control study. *Prog Urol.* 2018;28:530–5, <http://dx.doi.org/10.1016/j.purol.2018.07.001>.
 30. Nasimbera A, Rosales J, Silva B, Alonso R, Bohorquez N, Lepera S, et al. Everything you always wanted to know about sex and neurology: neurological disability and sexuality. *Arq Neuropsiquiatr.* 2018;76:430–4, <http://dx.doi.org/10.1590/0004-282X20180061>.
 31. Domingo S, Kinzy T, Thompson N, Gales S, Stone L, Sullivan A, et al. Factors associated with sexual dysfunction in individuals with multiple sclerosis: implications for assessment and treatment. *Int J MS Care.* 2018;20:191–7, <http://dx.doi.org/10.7224/1537-2073.2017-059>.
 32. Hösl KM, Deutsch M, Wang R, Roy S, Winder K, Niklewski G, et al. Sexual dysfunction seems to trigger depression in female multiple sclerosis patients. *Eur Neurol.* 2018;80:34–41, <http://dx.doi.org/10.1159/000492126>.
 33. Konstantinidis C, Tzitzika M, Bantis A, Nikolia A, Samarinas M, Kratiras Z, et al. Female sexual dysfunction among greek women with multiple sclerosis: correlations with organic and psychological factors. *Sex Med.* 2019;7, <http://dx.doi.org/10.1016/j.esxm.2018.11.003>.
 34. Tomé ALF, Miranda EP, de Bessa Júnior J, Bezerra CA, Pompeo ACL, Glina S, et al. Lower urinary tract symptoms and sexual dysfunction in men with multiple sclerosis. *Clin (Sao Paulo).* 2019;14:713, <http://dx.doi.org/10.6061/clinics/2019/e713>.
 35. Gava G, Visconti M, Salvi F, Bartolomei I, Seracchioli R, Meriggola MC, et al. Prevalence and psychopathological determinants of sexual dysfunction and related distress in women with and without multiple sclerosis. *J Sex Med.* 2019;16:833–42, <http://dx.doi.org/10.1016/j.jsxm.2019.03.011>.
 36. Ghasemi V, Simbar M, Ozgoli G, Nabavi SM, Majid AH. Prevalence, dimensions, and predictor factors of sexual dysfunction in women of Iran Multiple Sclerosis

- Society: a cross-sectional study. *Neurol Sci.* 2020;2, <http://dx.doi.org/10.1007/s10072-019-04222-6>.
37. Nazari F, Shaygannejad V, Mohammadi Sichani M, Mansourian MHV. Sexual dysfunction in women with multiple sclerosis: prevalence and impact on quality of life. *BMC Urol.* 2020;21:15, <http://dx.doi.org/10.1186/s12894-020-0581-2>.
 38. Baumstarck K, Boyer L, Boucekine M, Michel P, Pelletier J, Auquier P, et al. Measuring the quality of life in patients with multiple sclerosis in clinical practice: a necessary challenge. *Mult Scler Int.* 2013;2013:1–8, <http://dx.doi.org/10.1155/2013/524894>.
 39. Ware J, Snow K, Kosinski M, Gandek B. SF-36 health survey manual and interpretation guide. Boston, MA: New England Medical Center, The Health Institute; 1993.
 40. Vilagut G, Ferrer M, Rajmil L, Rebollo P, Permanyer-Miralda G, Quintana JM, et al. El Cuestionario de Salud SF-36 español: una década de experiencia y nuevos desarrollos. *Gac Sanit.* 2005;19:135–50, <http://dx.doi.org/10.1157/13074369>.
 41. Hellwig K, Brzosko B, Airas LSE. Health issues in women with multiple sclerosis. 1st ed. Wien: Springer-Verlag; 2017, <http://dx.doi.org/10.1007/978-3-7091-4858-7>.
 42. Vickrey BG, Hays RD, Harooni R, Myers LWEG. A health-related quality of life measure for multiple sclerosis. *Qual Life Res.* 1995;4:187–206.
 43. Cella DF, Dineen K, Arnason B, Reder A, Webster KA, Karabastos G, et al. Validation of the functional assessment of multiple sclerosis quality of life instrument. *Neurology.* 1996;47:129–39.
 44. Gold SM, Heesen CHS, Shulz H, Guder U, Mönch A, Gbadamosi J, et al. Disease specific quality of life instruments in multiple sclerosis: validation of the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS). *Mult Scler J.* 2001;7:119–30.
 45. Ferrans CE, Powers MJ. Psychometric assessment of the quality of life index. *Res Nurs Heal.* 1992;15:29–38.
 46. Fischer JS, LaRocca NG, Miller DM, Ritvo PGH, Andrews DP. Recent developments in the assessment of quality of life in Multiple Sclerosis (MS). *Mult Scler J.* 1999;5:251–9.
 47. Ford HL, Gerry E, Tennant A, Whalley D, Haigh R, Johnson MH. Developing a disease-specific quality of life measure for people with multiple sclerosis. *Clin Rehabil.* 2001;15:247–58, <http://dx.doi.org/10.1191/026921501673658108>.
 48. McGuigan C, Hutchinson M. The multiple sclerosis impact scale (MSIS-29) is a reliable and sensitive measure. *J Neurol Neurosurg Psychiatry.* 2004;75:266–9.
 49. Lankhorst GJ, Jelles F, Smits RC, Polman CH, Kuik DJ, et al. Quality of life in multiple sclerosis: the disability and impact profile (DIP). *J Neurol.* 1996;243:469–74.
 50. Schwartz CE, Cole BF, Gelber RD. Measuring patient-centered outcomes in neurologic disease: extending the QTWiST method. *Arch Neurol.* 1995;52:754–62.
 51. Simeoni M, Auquier P, Fernandez O, Flachenecker PSS. Validation of the Multiple Sclerosis International Quality of Life questionnaire. *Mult Scler.* 2008;14:219–30.
 52. Solà-Valls N, Vicente-Pascual M, Blanco Y, Solana E, Llufríu S, Martínez-Heras E, et al. Spanish validation of the telephone assessed Expanded Disability Status Scale and Patient Determined Disease Steps in people with multiple sclerosis. *Mult Scler Relat Disord.* 2019;27:333–9.
 53. Sharrack B, Hughes RAC. The Guy's Neurological Disability Scale (GNDS): a new disability measure for multiple sclerosis. *Mult Scler.* 1999;5:223–33.
 54. Lobo A, Chamorro L, Luque A, Dal-Ré R, Badia X, Baró E, et al. Validación de las versiones en español de la Montgomery-Asberg Depression Rating Scale y la Hamilton Anxiety Rating Scale para la evaluación de la depresión y de la ansiedad. *Med Clin (Barc).* 2002;118:480–520, [http://dx.doi.org/10.1016/S0025-7753\(02\)72429-9](http://dx.doi.org/10.1016/S0025-7753(02)72429-9).
 55. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977;1:385–401, <http://dx.doi.org/10.1177/014662167700100306>.
 56. Brookes S, Donovan J, Wright M, Jackson S, Abrams P. A scored form of the Bristol Lower Urinary Tract Symptoms questionnaire: data from a randomized controlled trial of surgery for women with stress incontinence. *Am J Obstet Gynecol.* 2004;191:73–82.
 57. Uebersax JS, Wyman JF, Shumaker SA, Mcclish DK. Short forms to assess life quality and symptom distress for urinary incontinence in women: the incontinence impact questionnaire and the urogenital distress inventory. *Neurourol Urodyn.* 1995;139:131–9.
 58. Patrick DL, Martin ML, Bushnell DM, Yalcin I, Wagner TH, Buesching DP, et al. Quality of life of women with urinary incontinence: further development of the incontinence quality of life instrument (I-QOL). *Urology.* 1999;53:71–6.
 59. Ritvo PG, Fischer JS, Miller DM, Andrew H, Paty DWLN. The multiple sclerosis quality of life inventory: a user's manual. New York, NY: National Multiple Sclerosis Society; 1997.